

### REQUEST FORM FOR FILE WRAPPER CONTINUING APPLICATION UNDER 37 CFR §1.62

A. FW

08/328,632 of Porubek et al. Prior Application:

Examiner: M. Berch Art Unit:

Attorney's Docket No.: 077319/0129

ADDRESS TO:

Assistant Commissioner for Patents Box FWC

Washington, D. C. 20231

This is a Request for filing a [ ] continuation-in-part, [x] continuation, [ ] divisional application under 37 CFR 1.62 of prior application Serial No. 08/328,632, filed on October 25, 1994, entitled COMPOUNDS HAVING SELECTIVE HYDROLYTIC POTENTIALS, by the following named inventor(s):

Full Name of David Porubek

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- 1 -

The above-identified prior application in which no payment of the issue fee, abandonment or, or termination of proceedings has occurred, is hereby expressly abandoned as of the filing date of this new application. Please use all the contents of the prior application file wrapper, including the drawings, as the basic papers for the new application. (Note: 37 CFR 1.60 may be used for applications where the prior application is not to be abandoned.)

- 1. [x] Enter the amendment previously filed on April 18, 1997, under 37 CFR 1.116, but unentered, in the prior application.
- 2. [x] A preliminary amendment is enclosed.
- 3. [x] The filing fee is calculated below. (Small entity fees indicated in parentheses.)

# CLAIMS AS FILED IN THE PRIOR APPLICATION LESS ANY CLAIMS CANCELED BY AMENDMENT BELOW

	<u>Number</u> <u>Filed</u>		<u>Number</u> Extra	<u>Rate</u>	Basic Fee \$770 (\$385)
Total Claims	20 - 2	20	0	x \$22 (x \$11)	-0-
Independent Claims	3 - 3	3	0	x \$80 (x \$40)	-0-
Multiple Dependent Claims				\$260 (\$130)	-0-
				TOTAL FEE	\$385.00

- 4. [] The Commissioner is hereby authorized to charge fees under 37 CFR 1.16 and 1.17 which may be required, or credit any overpayment to Deposit Account No. 19-0741.
- 5. [] A check in the amount of  $\frac{5-0}{}$  is enclosed.
- 6. [] A new oath or declaration is included since this application is a continuation-in-part which discloses and claims additional matter.

- 7. [X] Amend the specification by inserting before the first line the sentence:
  - --This application is a [] continuation-in-part, [x] continuation, [] division, of application Serial No. 08/328,632, filed October 25, 1994 which is a Continuation-In-Part of application Serial No. 08/306,091 filed on September 14, 1994, which is a Continuation-In-Part of application Serial No. 08/199,368 filed on February 18, 1994.--
- 8. [x] Small entity status, based on the verified statement filed in parent application Serial No. 08/328,632, filed October 25, 1994, is claimed under 37 CFR 1.28(a).
- 9. [x] Priority of application Serial No. 08/328,632 filed on October 25, 1994, in USA which is a Continuation-In-Part of application Serial No. 08/306,091 filed on September 14, 1994, in USA which is a Continuation-In-Part of application Serial No. 08/199,368 filed on February 18, 1994, in the USA is claimed under 35 USC 119.
- 10. [x] The prior application is assigned of record to: CELL THERAPEUTICS, INC.
- 11. [x] The power of attorney in the prior application is to: Stephen A. Bent, Reg. No. 29,768, and other members of the firm.
- 12. [ ] Also enclosed:

Address all further communications to: (May only be completed by applicant, or attorney or agent of record.)

FOLEY & LARDNER
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3000 K Street, N.W.
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### Attorney's Docket No. 077319/0129

It is understood that secrecy under 35 USC 122 is hereby waived to the extent that if information or access is available to any one of the applications in the file wrapper of a 37 CFR 1.62 application, be it either this application or a prior application in the same file wrapper, the Patent and Trademark Office may provide similar information or access to all the other applications in the same file wrapper.

September 18, 1997

Date

Stephen A. Bent Reg. No. 29,768

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#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 077319/0129

In re patent application of

David PORUBEK et al.

Group Art Unit: 1202

Continuation of Serial No. 08/328,632

Examiner: M.Berch

Filed: October 25, 1994

For: COMPOUNDS HAVING SELECTIVE HYDROLYTIC POTENTIALS

## PRELIMINARY AMENDMENT AND REQUEST FOR INTERVIEW

Assistant Commissioner for Patents Washington, D.C. 20231

sir:

Prior to examination on the merits, Applicants respectfully request an interview with the Examiner to discuss the merits of the case in view of the following preliminary amendment. Also before examination, please enter the following amendments.

#### IN THE CLAIMS

1. (Three Times Amended) A compound of formula I:

$$\begin{array}{c|c}
R_1 & & & \\
N & & \\
N & & & \\
N & &$$

wherein  $R_1$  has the formula II:

 $R_2$  and  $R_3$  are independently  $C_{(1-12)}$  alkyl, optionally,  $R_2$  having one or two nonadjacent carbon atoms of the  $C_{(1-12)}$  alkyl being replaced by an oxygen atom; and wherein:

C\* is a chiral carbon atom;

n is four;

 $R_4$  is a naturally occurring amino acid or carbohydrate-moiety attached by an oxygen atom to the chiral carbon atom C\* by an ester linkage,  $-O-X-(R_7)_2$  or  $-O-X-(R_5)_m$ ; m being two or three and X being selected from the group consisting of C, P or S; wherein [:  $R_5$ ]  $R_7$  is a member independently selected from the group consisting of Group Q, hydrogen, and dimethylamino, wherein when one  $R_7$  is dimethylamino, the other  $R_7$  is =0, n is 4, X is C and  $R_2$  and  $R_3$  are both methyl, and wherein  $R_5$  is a member independently selected from Group Q, and

#### Group Q consists of:

[hydrogen atom, wherein no more than two  $R_5 s$  are hydrogen;] hydroxyl group;

=0;

[dimethylamino;]

substituted or unsubstituted  $C_{(3-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkenyl,  $C_{(1-10)}$  alkynyl,  $C_{(1-10)}$  alkoxyl,  $C_{(1-10)}$  oxoalkyl, [or  $C_{(1-10)}$  acetoxyalkyl],  $C_{(1-10)}$  carboxyalkyl,  $C_{(1-10)}$  hydroxyalkyl, or substituted  $C_{(1-2)}$  alkyl group;

-OR, R, being a substituted or unsubstituted  $C_{(1-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkynyl, or  $C_{(1-10)}$  oxoalkyl;

substituted or unsubstituted heterocylic group having one or two rings, each ring containing from four to seven atoms, wherein the heteroatom(s) of said heterocyclic group is 1 or 2 nitrogens; and

substituted or unsubstituted carbocyclic group <u>that is</u> <u>attached to X through a carbon atom within a ring</u>, having one or two rings, each ring containing [from] four to seven atoms, wherein the substituents of said substituted carbocyclic group are selected from the group consisting of amino,  $C_{(2-6)}$  alkenyl,  $C_{(1-6)}$  alkyl,  $C_{(1-6)}$  alkoxyl,  $C_{(1-6)}$  hydroxyalkyl, hydroxyl,  $C_{(1-6)}$  oxoalkyl, azido, carboxy, cyano,  $C_{(2-6)}$  mono- or di-haloalkyl, isocyano, isothiocyano, [phospho, phosphono, sulfonato,]

alkylphospho, alkylphosphono, alkylsulfoxy, imino, [thioalkoxyl]
alkylthio, a chlorine atom, a bromine atom, a fluorine atom and
an oxygen atom.

- 6. (Three Times Amended) The compound of claim 1, wherein substituents for the substituted  $C_{(1-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkynyl,  $C_{(1-10)}$  alkoxyl,  $C_{(1-10)}$  oxoalkyl, [or  $C_{(1-10)}$  acetoxyalkyl,] or heterocylic groups [are] selected from the group consisting of amino,  $C_{(2-6)}$  alkenyl,  $C_{(1-6)}$  alkyl,  $C_{(1-6)}$  alkoxyl,  $C_{(1-6)}$  hydroxyalkyl,  $C_{(1-6)}$  oxoalkyl, azido, carboxy, cyano,  $C_{(1-6)}$  haloalkyl, isocyano, isothiocyano, [phospho, phosphono, sulfonato,] alkylphospho, alkylphosphono, alkylsulfoxy, imino, [thioalkoxyl] alkylthio, or a chlorine, bromine fluorine and oxygen atom.
- 10. (Three Times Amended) The compound of claim 1, wherein the cyclic or heterocyclic is selected from the group consisting biphenyl, benzyl, phenyl, cyclohexyl, cyclohexenyl, cyclopentyl, nicotinyl, cyclopentenyl, cyclopentanedionyl, napthlalenyl, phenolyl, quinonyl, cyclobutyl, cycloheptyl, cycloheptenyl, indanyl, indenyl, decalinyl, resorcinolyl,  $\alpha$ -tetralonyl, 1-indanonyl, cyclohexanedionyl, tetralinyl, cyclopentanedionyl, dimethylxanthinyl, methylxanthinyl, phthalimidyl, homophthalimidyl, [methylbenzoyleneurea-moiety,] quinazolinonyl, octylcarboxamidophenyl, [N-methylbenzamido, 1methyl-2,4-dioxotetrahydropteridyl,] glutarimidyl, piperidonyl, dimethoxyphenyl, methyldihydrouracilyl, succinimidyl, methyluracilyl, methylthyminyl, piperidinyl, dihydroxybenzenyl, methylpurinyl, methylxanthinyl and dimethylxanthinyl.
- 12. (Twice Amended) The compound of claim 11, wherein the other  $R_5$ , other than =0, is selected from the group consisting of trimethoxy-substituted phenyl, [hydroxyphenyl] and [aminophenyl] phenylamino.

15. (Three Times Amended) A pharmaceutical composition comprising a pharmaceutically acceptable excipient or carrier and a compound having the following formula I:

$$\begin{array}{c|c}
R_1 & & \\
N & & \\
N & & \\
N & & \\
R_2 & & 
\end{array}$$

wherein  $R_1$  has the formula II:

 $R_2$  and  $R_3$  are independently  $C_{(1-12)}$  alkyl, optionally,  $R_2$  having one or two nonadjacent carbon atoms of the  $C_{(1-12)}$  alkyl being replaced by an oxygen atom; and wherein:

C\* is a chiral carbon atom;
n is four;

 $R_4$  is a naturally occurring amino acid or carbohydrate-moiety attached by an oxygen atom to the chiral carbon atom C\* by an ester linkage,  $-O-X-(R_7)_2$  or  $-O-X-(R_5)_m$ ; m being two or three and X being selected from the group consisting of C, P or S; wherein [:  $R_5$ ]  $R_7$  is a member independently selected from the group consisting of Group Q, hydrogen and dimethylamino, wherein when one  $R_7$  is dimethylamino, the other  $R_7$  is =0, n is 4, X is C and  $R_2$  and  $R_3$  are both methyl, and wherein  $R_5$  is a member independently selected from Group Q, and

#### Group Q consists of:

[hydrogen atom, wherein no more than two  $R_{\scriptscriptstyle 5}s$  are hydrogen;] hydroxyl group;

=0;

dimethylamino, wherein, when one  $R_5$  or  $R_7$  is dimethylamino, m and z are two, the other  $R_5$  or  $R_7$  is =0, n is 4, X is C and  $R_2$  and  $R_3$  are both methyl;

substituted or unsubstituted  $C_{(3-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkenyl,  $C_{(1-10)}$  alkynyl,  $C_{(1-10)}$  alkoxyl,  $C_{(1-10)}$  oxoalkyl, [or  $C_{(1-10)}$  acetoxyalkyl,]  $C_{(1-10)}$  carboxyalkyl,  $C_{(1-10)}$  hydroxyalkyl, or substituted  $C_{(1-2)}$  alkyl group;

-OR, R, being a substituted or unsubstituted  $C_{(1-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkynyl, or  $C_{(1-10)}$  oxoalkyl;

substituted or unsubstituted heterocylic group that is attached to X through a carbon atom within a ring, having one or two rings, each ring containing [from] four to seven atoms, wherein the heteroatom(s) of said heterocyclic group is 1 or 2 nitrogens; and

substituted or unsubstituted carbocyclic group, having one or two rings, each ring containing from four to seven atoms, wherein the substituents of said substituted carbocyclic group are selected from the group consisting of amino,  $C_{(2-6)}$  alkenyl,  $C_{(1-6)}$  alkyl,  $C_{(1-6)}$  alkoxyl,  $C_{(1-6)}$  hydroxyalkyl, hydroxyl,  $C_{(1-6)}$  oxoalkyl, azido, carboxy, cyano,  $C_{(2-6)}$  mono- or di-haloalkyl, isocyano, isothiocyano, [phospho, phosphono, sulfonato,] alkylphospho, alkylphosphono, alkylsulfoxy, imino, [thioalkoxyl] alkylthio, a chlorine atom, a bromine atom, a fluorine atom and an oxygen atom.

20. (Twice Amended) A compound of formula I:

wherein [one of]  $R_1$  or  $R_2$  has the formula II:

 $R_1$  or  $R_2$ , which is other than formula II, and  $R_3$  are independently  $C_{(1-12)}$  alkyl, optionally,  $R_2$  having one or two nonadjacent carbon atoms of the  $C_{(1-12)}$  alkyl being replaced by an oxygen atom; and wherein:

C\* is a chiral carbon atom;
n is four;

 $R_4$  is a naturally occurring amino acid or carbohydrate-moiety attached by an oxygen atom to the chiral carbon atom C\* by an ester linkage,  $-O-X-(R_7)_2$  or  $-O-X-(R_5)_m$ ; m being two or three and X being selected from the group consisting of C, P or S; wherein [:  $R_5$ ]  $R_7$  is a member independently selected from the group consisting of Group Q, hydrogen and dimethylamino, wherein when one  $R_7$  is dimethylamino, the other  $R_7$  is =O, n is 4, X is C and  $R_2$  and  $R_3$  are both methyl, and wherein  $R_5$  is a member independently selected from Group Q, and

#### Group Q consists of:

[hydrogen atom, wherein no more than two  $R_{\scriptscriptstyle 5}s$  are hydrogen;] hydroxyl group;

=0;

dimethylamino, wherein, when one  $R_5$  or  $R_7$  is dimethylamino, m and z are two, the other  $R_5$  or  $R_7$  is =0, n is 4, X is C and  $R_2$  and  $R_3$  are both methyl;

substituted or unsubstituted  $C_{(3-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkenyl,  $C_{(1-10)}$  alkynyl,  $C_{(1-10)}$  alkoxyl,  $C_{(1-10)}$  oxoalkyl, [or  $C_{(1-10)}$  acetoxyalkyl,]  $C_{(1-10)}$  carboxyalkyl,  $C_{(1-10)}$  hydroxyalkyl, or substituted  $C_{(1-2)}$  alkyl group;

-OR<sub>6</sub>, R<sub>6</sub> being a substituted or unsubstituted  $C_{(1-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkynyl, or  $C_{(1-10)}$  oxoalkyl;

substituted or unsubstituted heterocylic group having one or two rings, each ring containing from four to seven atoms,

wherein the heteroatom(s) of said heterocyclic group is 1 or 2 nitrogens; and

substituted or unsubstituted carbocyclic group <u>that is</u> <u>attached to X through a carbon atom within a ring</u>, having one or two rings, each ring containing [from] four to seven atoms, wherein the substituents of said substituted carbocyclic group are selected from the group consisting of amino,  $C_{(2-6)}$  alkenyl,  $C_{(1-6)}$  alkyl,  $C_{(1-6)}$  alkoxyl,  $C_{(1-6)}$  hydroxyalkyl, hydroxyl,  $C_{(1-6)}$  oxoalkyl, azido, carboxy, cyano,  $C_{(2-6)}$  mono- or di-haloalkyl, isocyano, isothiocyano, [phospho, phosphono, sulfonato,] <u>alkylphospho, alkylphosphono, alkylsulfoxy</u>, imino, [thioalkoxyl] <u>alkylthio</u>, a chlorine atom, a bromine atom, a fluorine atom and an oxygen atom.

Please add the following new claims:

-- 21. A compound according to claim 1, wherein  $\rm R_2$  and  $\rm R_3$  are methyl, and wherein  $\rm R_6$  is a

substituted or unsubstituted  $C_{(1-10)}$  alkyl,  $C_{(2-10)}$  alkenyl,  $C_{(2-10)}$  alkynyl, or  $C_{(1-10)}$  oxoalkyl;

substituted or unsubstituted heterocylic group having one or two rings, each ring containing from four to seven atoms, and a single nitrogen as the heteroatom; or

substituted or unsubstituted carbocyclic group that is attached to X through a carbon atom within a ring, having one ring containing four to seven atoms, wherein the substituents of said substituted carbocyclic group are selected from the group consisting of amino,  $C_{(2-6)}$  alkenyl,  $C_{(1-6)}$  alkyl,  $C_{(1-6)}$  alkoxyl,  $C_{(1-6)}$  hydroxyalkyl, hydroxyl,  $C_{(1-6)}$  oxoalkyl, azido, carboxy, cyano,  $C_{(2-6)}$  mono- or di-haloalkyl, isocyano, isothiocyano, imino, a chlorine atom, a bromine atom, a fluorine atom and an oxygen atom.

22. A compound according to claim 21, wherein one  $R_7$  is =0 and wherin one  $R_5$  is =0. --

#### REMARKS

Applicants hereby request examination of the present application in view of the foregoing amendments and the following remarks. The amendments to the existing claims are directly in response to Applicants' July 10, 1997 interview with Examiner Berch, and find full support in the original claims and the specification. The are presented solely for clarification of nomenclature. New claims 21 and 22 find support in claim 1. No new matter is presented. Upon entry of the foregoing amendments, claims 1-7 and 9-21 will be pending.

In view of the foregoing, Applicants submit that the present claims are in condition for allowance. Should the Examiner have any questions regarding the present application or believe that further discussion will advance prosecution, the Examiner is invited to contact the undersigned at the number listed below.

Respectfully submitted,

Lt September 1997

Stephen A. Bent Reg. No. 29,768

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